Amendments to the Specification:

Please replace the paragraph beginning at page 8, line 17, with the following redlined paragraph:

The peptide may bind to one or both of the carboxy-or amino-terminal domains of the a-chain of fibrinogen. More particularly, the peptide may bind to an RGD-containing motif in one or both of said domains. The RGD-containing motif may have the sequence RGDX (SEQ ID NO: 1), where X is any amino acid, such as serine, valine, phenylalanine or alanine, and thus may be RGDF at amino acids 95-98, or RGDS at amino acids 572-575.

Please replace the paragraph beginning at page 8, line 24, with the following redlined paragraph:

The peptide may bind to the C-terminal domain of the y-chain of fibrinogen. More particularly the peptide may bind to a sequence within the final 15, 12,10 or 4 amino acids of the C-terminal domain of the fibrinogen y-chain. The final 12 amino acids are usually HHLGGAKQAGDV (SEQ ID NO: 4).

Please replace the paragraph beginning at page 13, line 1, with the following redlined paragraph:

Thus the fibrinogen-binding peptide may comprise the sequence of AVTDVNGDRHDLLVGAPLYM (SEQ ID NO: 5), which represents the sequence of amino acids 294-314 of GPIIb, or a fibrinogen-binding fragment thereof. Such fragments include the sequence TDVNGDGRHDL (296-306) (SEQ ID NO: 6), the sequence GDGRHDLLVGAPL (300-312) (SEQ ID NO: 7) and the terminal tetrapeptide GALP (SEQ ID NO: 27). These sequences are thought to be involved in the binding of

fibrinogen and, in particular, the γ-chain of fibrinogen (Bennett, 2001, op. cit.; D'Souza ~~*et al*~~ et al., 1991, *Nature*, 350, 66-68 ; Taylor & Gartner, 1992, *J. Biol. Chem.*, 267,11729-33). The similar effects of fragments 296-306 and 300- 312 suggest that fragment 300-306 may also provide fibrinogen-binding activity.

Please replace the paragraph beginning at page 13, line 14, with the following redlined paragraph:

Grunkemeier ~~*et al*~~ et al. (1996, *J. Molecular Recognition*, 9, 247-257) reported that purified TDVNGDGRHDL (SEQ ID NO: 12) (designated"B12") peptide caused inhibition of platelet aggregation. Grunkemeier ~~*et al*~~ et al. used this information to propose non-platelet-adhesive materials coated in B12 peptide, and hypothesised that B12 would bind fibrinogen specifically in the region that binds to the GPIIb/IIIa platelet receptor, thus blocking platelet aggregation. Therefore, the understanding in Grunkemeier ~~*et al*~~ et al. -is that, when immobilised, the B12 peptide can be used to block fibrinogen binding to platelets, and thus inhibit platelet aggregation. In light of this teaching, it was not apparent that the B 12 peptide would be suitable for use in a platelet substitute for aiding platelet aggregation and blood clot formation.

Please replace the paragraph beginning at page 13, line 26, with the following redlined paragraph:

The fibrinogen-binding peptide may comprise one or more of the peptides APLHK (SEQ ID NO: 9), EHIPA (SEQ ID NO: 10) and GAPL (SEQ ID NO: 8) which were shown in Gartner, 1991, *Biochem. Biophys. Res. Commun.*, 180(3), 1446-52 to be hydropathically equivalent peptide mimics of the fibrinogen binding domain of GPIIb-IIIa. The fibrinogen-binding peptide may comprise the sequence of residues 95- 223 of GPIIIa or a fibrinogen-binding fragment thereof. For example, residues 211-222, comprising the sequence SVSRNRDAPEGG (SEQ ID NO: 11) is thought to be an

important fibrinogen-binding domain in GPIIIa (Charo ~~*et al*~~ et al., 1991, *J. Biol. Chem.*, 266,1415-1421).

Please replace the paragraph beginning at page 14, line 13, with the following redlined paragraph:

A particularly preferred fibrinogen-binding peptide comprises a sequence obtained from the platelet membrane glycoprotein GPIIb, namely TDVNGDGRHDL (SEQ ID NO: 12), or a variant of such a sequence.

Variants of TDVNGDGRHDL (SEQ ID NO: 12) include-

T(D,E)VNG(D,E)GRH(D,E)L (SEQ ID NO: 28)
TD(V,L)NGDGRHDL (SEQ ID NO: 29)
TDV(N,Q)GDGRHDL (SEQ ID NO: 30)
TDVNGDG(R,K)HDL (SEQ ID NO: 31)

Please replace the paragraph beginning at page 14, line 23, with the following redlined paragraph:

Such variants will have substantially the same fibrinogen binding activity as TDVNGDGRHDL (SEQ ID NO: 12), in that they will have substantially the same affinity for fibrinogen and, when bound, fibrinogen will have substantially the same conformation and activity as when bound to TDVNGDGRHDL (SEQ ID NO: 12). By "substantially the same fibrinogen-binding activity" we include variants that bind fibrinogen with an affinity up to 1, 2,3, 4,5, 10, 50, 100 or more orders of magnitude different (either higher or lower) to TDVNGDGRHDL (SEQ ID NO: 12). Lower numbers are preferred.

Please replace the paragraph beginning at page 15, line 1, with the following redlined paragraph:

Kuyas ~~*et al*~~ *et al.* 1990, *Thrombosis and Haemostasis*, 63(3), 439, describes the use of the synthetic peptide GPRPK (SEQ ID NO: 16), immobilised via the C-terminal lysine to fractogel, to isolate fibrinogen from human plasma. Kuyas ~~*et al*~~ et al. explains that human fibrinogen has a strong affinity for fibrin, and reports that the authors utilised a peptide comprising the N-terminal sequence of the a- chain of fibrin exposed by the action of thrombin, GPRP (SEQ ID NO: 17), which had been shown to bind fibrinogen (Laudano & Doolittle, 1980, *Biochemistry*, 19, 1013; Laudano ~~*et al*~~ et al. 1983, *Ann. N. Y. Acad. Sci.*, 408,315). Kuyas ~~*et al*~~ et al. concludes that the 'core' sequence GPR is required for fibrinogen binding.

Please replace the paragraph beginning at page 15, line 12, with the following redlined paragraph:

Thus, the fibrinogen-binding peptide as used in the product may comprise the sequence of a fibrinogen-binding region of fibrin such as the N-terminal region of the a-chain or the C-terminal region of the ß-chain. Accordingly the peptide may have the sequence Gly-(Pro/His/Val)-Arg-Xaa (SEQ ID NO: 32) at the amino terminus, wherein Xaa is any amino acid. In this context, by "at the amino terminus"we mean that the Gly residue in the above tetrapeptide sequence should represent the first amino acid of the peptide when read from the N- terminus to the C-terminus. By"Pro/His/Val" we mean that either proline, histidine or valine is included at that position. In one embodiment, proline and histidine are preferred, and proline is most preferred.

Please replace the paragraph beginning at page 15, line 28, with the following redlined paragraph:

The peptide may comprise the sequence of Gly-Pro-Arg-Pro (SEQ ID NO: 17) at the amino terminus. Alternatively, the peptide may comprise the sequence of Gly-Pro-Arg-Sar (SEQ ID NO: 33) (Sar is short for sarcosine, which is methyl glycine), Gly-

Pro-Arg-Gly (SEQ ID NO: 34) or Gly-Pro-Arg-Val (SEQ ID NO: 35) at the amino terminus.

Please replace the paragraph beginning at page 23, line 17, with the following redlined paragraph:

Any variant or fragment of fibrinogen may be used, provided that it has a useful level of inducible platelet-aggregating activity. In this context, a useful level of inducible platelet-aggregating activity means that the variant or fragment can be used with the product of the invention to cause aggregation of activated platelets in preference to inactive platelets, as described above. Preferably, any such variant or fragment includes residues 398-411 of the gamma chain of fibrinogen. In a preferred embodiment, the variant or fragment may include, or even consist of, HHLGGAKQADV (SEQ ID NO: 20).

Please replace the paragraph beginning at page 28, line 21, with the following redlined paragraph:

(iii) The pellet was resuspended in 1 ml of a suitable buffer such as phosphate buffered saline. The peptide (either GPRPC (SEQ ID NO: 21), GPRPGGGC (SEQ ID NO: 22) or GPRPGGGGGGC (SEQ ID NO: 23)), supplied by Merck Biosciences, was dissolved in phosphate buffered saline and added to the microspheres at a final concentration of 0. 23mM. This was mixed at room temperature for 24 hours. An appropriate negative control was provided by treating the preparation with 0.23mM L-cysteine (cysteine control). A wash was performed by centrifuging at 3000 x g for 5 minutes and resuspending in phosphate buffered saline. The washing step was repeated twice, followed by resuspension finally in a volume of 1 ml.

Please replace the paragraph beginning at page 30, line 7, with the following redlined paragraph:

The products made by method 1 above were tested using method 2. Specifically the products tested had, as the bound peptide, either"peptide Gly"=0" (i. e. GPRPC (SEQ ID NO: 21)),"peptide Gly"=3" (i.e. GPRPGGGC (SEQ ID NO: 22)) or"peptide Glyn=6" (i.e. GPRPGGGGGGC (SEQ ID NO: 23)). A cysteine control sample was also included. The results are reported in Table 1 below.

Please replace the paragraph beginning at page 31, line 5, with the following redlined paragraph:

Product 1 : Artificial Platelets were produced, using the peptide GPRPGGGGGGC (SEQ ID NO: 23) (i. e. $Gly^n = 6$) with bound fibrinogen, using steps (i) to (iv) of method 1 of Example 1, as discussed above, except that step (iv) used 0.1 mg/ml of fibrinogen, rather than 3 mg/ml.

Please replace the paragraph beginning at page 31, line 10, with the following redlined paragraph:

Product 2: Artificial Platelets were produced, using the peptide GPRPGGGGGGC (SEQ ID NO: 23) (i. e. $Gly^n = 6$) without fibrinogen, using steps (i) to (iii) of method 1 as discussed above.

Please replace the paragraph beginning at page 32, line 15, with the following redlined paragraph:

In summary, product 1 is a FLP (fibrinogen-linked particle) of the invention having fibrinogen bound via the peptide GPRPGGGGGGC (SEQ ID NO: 23), the peptide being bound to the microsphere. Product 2 is identical to product 1 except that it has no fibrinogen bound to the peptide GPRPGGGGGGC (SEQ ID NO:23). The

reference product has fibrinogen bound directly to the surface of the microsphere, in the manner known from the prior art, such as in WO 98/17319 and Davies ~~et al~~ et al., supra.

Please replace the paragraph beginning at page 33, line 12, with the following redlined paragraph:

To determine the effect of fibrinogen concentration on activity of products of the invention, microspheres were prepared using DNTB to link GPRPGGGGGGC (SEQ ID NO: 23) according to the method described above.

Please delete the section of the application entitled "Sequence Listing" immediately after Claim 60 and insert the enclosed Sequence Listing therefor.